



DEPARTMENT OF HEALTH & HUMAN SERVICES

HFI-35429  
3/3/97  
Public Health Service

Mid-Atlantic Region

D1273B

Telephone (201) 331-2905

Food and Drug Administration  
Waterview Corporate Center  
10 Waterview Blvd., 3rd Floor  
Parsippany, NJ 07054

March 19, 1997

**WARNING LETTER**

Mr. Robert C. Strauss  
President  
Cordis Corporation  
5200 Blue Lagoon Drive  
Miami, Florida 33126

Reviewed by

C.O.

DTE

CFN: 2247023

File No: 97-NWJ-24

Dear Mr. Strauss:

During an inspection of your facility located at 35 Technology Drive, Warren, New Jersey, which was initiated on 12/11/96 and concluded 1/16/97, our investigators determined that your firm manufactures the Palmaz-Schatz balloon expandable coronary stent delivery system. This is a device as defined by Section 201(h) of the Federal Food, Drug and Cosmetic Act (the Act).

The above-stated inspection revealed that this device is adulterated within the meaning of section 501(h) of the Act, in that the methods used in, or the facilities or controls used for manufacturing, packing, storage, or installation are not in conformance with the Good Manufacturing Practice (GMP) for Medical Devices Regulation, as specified in Title 21, Code of Federal Regulations (CFR), Part 820. The deviations were noted on the FDA-483 presented to your firm at the close of the inspection on January 16, 1997. The significant observations are as follows:

1. Complaints of device failures lacked documentation of adequate follow-up investigations into why the failures occurred. These include:

A. The evaluation of complaint numbers 96-1861 dated 7/22/96, 96-2661 dated 10/9/96, 96-2762 dated 10/18/96 and 96-1494 dated 6/10/96 which concerned stent movement.

B. The evaluation of complaint numbers 96-1860 dated 7/22/96 and 96-1284 dated 5/6/96 which confirmed the reports of tracking problems.

C. The evaluation of complaint numbers 96-2052 dated 8/9/96, 96-2579 dated 9/26/96, 96-1747 dated 7/10/96, 96-2522 dated 9/19/96, 96-1497 dated 6/10/96, and 96-1610 dated 6/19/96 which confirmed the reports of sheath difficulty.

D. The evaluation of complaint numbers 96-1864 dated 7/22/96, 96-1493 dated 6/7/96, 96-2019 dated 8/6/96, 96-1199 dated 5/8/96, 96-

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2145 dated 8/19/96, and 96-2141 dated 8/13/96 which confirmed the reports of balloon rupture/tear/inflation problems. Other complaints include 96-2412 dated 9/12/96 and 96-2594 dated 9/30/96.

2. The validation of the balloon forming machines conducted from April 1995 to February 12, 1996 is inadequate due to the following:

A. The Programmable Logic Controller which controls the balloon forming machine was not qualified.

B. There is no documentation that the low, nominal and high settings, which were not specified by numbers, were performed with product meeting all of the firm's specifications. The initial Performance Qualification dated April 10, 1995 was performed on the balloon forming machines at low, nominal and high ranges. The strength, length, distal and proximal ID were not all within tolerances and had to be re-run. After performing another test with 40 low, 40 nominal and 40 high, it was concluded "the length measurements and some burst strengths, double wall thicknesses, distal diameters and proximal diameters did not meet specifications". This test was conducted again with 10 samples per group and it was concluded "Most lengths, some burst strengths, distal...did not meet requirements". . . .

C. The lot numbers of product used in the performance qualification testing were not recorded on the data pages in Performance Qualification Supplement #1 dated 10/02/95, nor was there a device history record showing that the balloons were sterilized. This Supplement was done at one setting for the balloon machine. During this and subsequent protocols for the 3.0 mm balloon, length was not recorded.

D. The Performance Qualifications Supplement #1 states that the purpose of the protocol is to show the process..."can consistently produce balloons that meet all dimensional and functional requirements". The conclusion states "1 out of 37 catheters had double wall thickness of .0042 which is above the tolerance. Also, the results for proximal ID showed that 11 of 37 catheters were less than the as-formed requirement".

E. Burst testing was not done on balloons where distal ID, proximal ID, double wall and inflated diameter were measured. There is also no record of equipment settings during execution of the protocol.

F. There are no specifications for equipment settings on the balloon forming machines. The written procedure for balloon

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formation, #PS-B002, indicates these settings are guides and may be increased or decreased to obtain balloon specifications from lot to lot of material. Data collected shows that temperatures ranged from 250°F to 320°F; the pressure varied from 65-90 PSI, the stretch from 1.3 to 1.8 cm and the heater height varied from 11.0 to 11.2 cm.

3. There is no assurance that the inner member process will consistently yield product which meets pre-determined specifications when the temperature ranges which are specified in the Extrusion Procedure #PS-E007 are used. For example:

A. There is no documentation to support the specifications for extrusion settings in Document #PS-E007 dated 10/14/96. Specifically: Zone #1 can be set at 315°-345°, Zone #2 at 345°-375°, Zone #3 at 380°-410°, Die #1 at 405°-435°, Die #2 at 420°-450°, Die #3 at 505°-535°, the Take-up speed at 15-65 ft/min and the Melt temperature at 415°-455°. These parameters were not varied in the production qualification dated 11/12/96.

B. In the production qualification, it states "The remaining inner members were then subjected to a secondary leak test and visual inspection based on a zero acceptance criteria." The conclusion states "of the 11 rejects from the Secondary Leak test...there were three true inner member rejects (2 leaks + 1 visual)...all acceptance criteria except one was successfully met..."

C. There is no documentation that outer diameter was measured during the production qualification runs.

D. On 1/3/97, a new procedure was written which eliminates the firm's previous specifications for equipment settings. These settings are now references.

4. There is no assurance that the balloon tubing extrusion method is capable of producing product which meets pre-determined specifications due to the following:

A. In the firm's procedure for Extrusion of Polyethylene Balloon Tubing dated 10/14/96, there are no specifications for the extruder. The settings for the equipment parameters such as Zone #1, 2, 3; Die #1, 2, 3, 4, 5 and Puller Speed are listed as guidelines. These parameters were not varied in the firm's production qualification dated 11/12/96.

B. There is no specification or guideline for the melt temperature of the resin.

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5. There is no assurance that the incoming testing for the tuohy-borst valve is capable of detecting bad valves. The incoming testing simply involves verifying the name and catalogue number on the outside box. There were several confirmed complaints involving sheath movement, even when the tuohy-borst valve was tightened down.

6. The incoming specification for Kynar resin lists the specific gravity as 1.78@23°C, but the manufacturer's certification does not provide specific gravity. Also, the incoming specification for polyethylene resin used in balloon tubing specifies that the product has a melting point of 110° - 140°C; the certification does not provide the melting point of the resin.

This letter is not intended to be an all-inclusive list of deficiencies at your facility. It is your responsibility to ensure adherence to each requirement of the Act and regulations. The specific violations noted in this letter and in the FDA 483 issued at the closeout of the inspection are similar to deficiencies noted during previous inspections and may be symptomatic of serious underlying problems in your firm's manufacturing and quality assurance systems. You are responsible for investigating and determining the causes of the violations identified by the FDA. If the causes are determined to be systems problems, you must promptly initiate permanent corrective actions.

We acknowledge that a response dated January 27, 1997 has been submitted to this office concerning the observations noted on the form FDA 483. A review has been conducted by this office and comments of major concern follow:

1) Regarding the balloon forming process, a review of device history records does not provide data on worst case situations or define how the critical parameters interact with one another. The justification as to why the decrease in proximal ID would not effect the functionality of the device is not clear. The response does not give sufficient detail of the data upon which this conclusion is based.

2) With regard to balloon burst testing, we agree that distal ID, proximal ID, and double wall measurements would not be feasible on the same balloons where burst testing was done. Such testing should have been done separately on balloons from the same production run or lot which used the same raw material.

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3) The lack of specific equipment settings for balloon forming is a concern. The response does not address why a raw material, which should have specific attributes, is causing such wide variations in processing parameters.

4) Regarding the inner member extrusion process, our concern, as it is for the balloon forming process, is that specific, properly validated process parameters be identified. The response identifies melt temperature as a critical factor but not line speed. It is not clear if the new study will take into account the line speed as regards the inner member coating process and any effect temperature variations may have.

5) Regarding the balloon tubing extrusion process, the response indicates the instructions will be amended to provide tolerances around the temperatures listed and the puller speed. It is not clear how tolerances can be set up when the temperature settings were not varied during production qualification.

We also acknowledge receipt of a letter dated March 18, 1997 from Mr. William D. Schaeffer, Vice President, Quality Assurance Worldwide summarizing corrective actions being taken. These will be reviewed and comments will follow separately.

Federal agencies are advised of the issuance of all Warning Letters about devices so that they may take this information into account when considering the award of contracts. Additionally, no premarket submissions for devices to which the GMP deficiencies are reasonably related will be cleared until the violations have been corrected. Also, no requests for Certificates For Products For Export will be approved until the violations related to the subject devices have been corrected.

In order to facilitate FDA in making a determination that corrections have been made and thereby enabling FDA to withdraw its advisory to other federal agencies concerning the award of government contracts and to resume marketing clearance for 510(k) approvals, we are requesting that you submit to this office on the schedule below, certification by an outside consultant that an audit of your firm's quality assurance system has been conducted, relative to the requirements of the device GMP regulation (21CFR, Part 820). You should also submit certification, as the firm's president, that you have reviewed the consultant's report and that your firm has initiated or completed all corrections called for in the report.

The initial certifications of updated audits and corrections and subsequent certifications of updated audits and corrections should be submitted to Office of the District Director (currently vacant)

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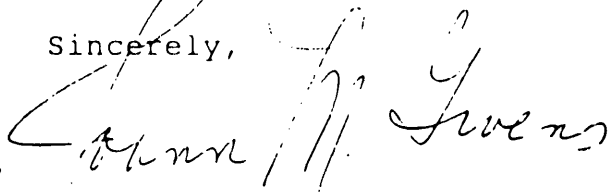
of the New Jersey District Office, Food and Drug Administration, by the following dates:

- Initial certification by consultant and firm due by September 30, 1997
- Subsequent certification due by December 31, 1997, annual recertification due by March 31, 1998

You should take prompt action to correct these deviations. Failure to promptly correct these deviations may result in regulatory action being initiated by the Food and Drug Administration without further notice. These actions include, but are not limited to, seizure, injunction, and/or civil penalties.

It is requested that you, or your designated agent, contact this office within 15 work days of receipt of this letter to set up a meeting to discuss these matters at your earliest convenience. Correspondence concerning your response should be sent to Richard T. Trainor, Compliance Officer, Food and Drug Administration, 10 Waterview Blvd., 3rd Floor, Parsippany, New Jersey 07054.

Sincerely,

  
Paul D'Eramo  
Acting, District Director  
New Jersey District

CERTIFIED MAIL -  
RETURN RECEIPT REQUESTED

RTT:np

cc: Mr. William D. Schaeffer  
Vice President of Quality Assurance Worldwide  
Cordis  
40 Technology Drive  
Warren, New Jersey 07059